DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20856

Ms. Charmaine Henderson
Director, Regulatory Affairs and Quality Assurance
Alliance Medical Technologies, Inc.
17590 Gillette Avenue
Irvine, California 92614

SEP 30 1997

Re: P970002
Monostrut™ Cardiac Valve Prosthesis
Filed: January 24, 1997
Amended: January 28, 31, February 12, March 5, 6, 10, and 17, August 21, September 18 (two amendments), 23 (two amendments), 24 (two amendments), 26 (five amendments), and 30, 1997

Dear Ms. Henderson:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Monostrut™ Cardiac Valve Prosthesis. This device is indicated for the replacement of malfunctioning native or prosthetic mitral (sizes 27, 29, 31,and 33 mm) or aortic (sizes 21, 23, 25, 27, 29, 31, and 33 mm) heart valves. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, your postapproval study should collect 10 year follow-up data on a statistically valid sample size in order to evaluate complication rates and to determine the long-term durability of the valve. Your protocol must be submitted, as a PMA supplement, within 60 days of the date of this letter. You may use the current Canadian Cohorts 1 and 2, if an adequate number of patients remain at 10 years.

The postapproval study should capture the following information at a minimum:

(1) rates of complications, specifically: thromboembolism; perivalvular leak; thrombosis; death; and reoperation (autopsies and explant analyses are to be reviewed by a core pathologist); (2) New York Heart Association classification; (3) anticoagulation status and adequacy of the regimen; and (4) annual echocardiographic assessments. This information should be submitted on an annual basis.

Expiration dating for this device has been established and approved at 5 years.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

In addition under section 522(a) of the Federal Food, Drug, and Cosmetic Act, (the act) manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted device as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

At that time you should submit five (5) copies to:

Postmarket Studies Document Center
1350 Piccard Drive (HFZ-544)
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522.

In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the Federal Food, Drug and Cosmetic Act (the act)(21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA.

If you have any questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639.

Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your device is a device that is subject to tracking because it is a permanent implant whose failure would be reasonably likely to have serious adverse consequences.

FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR § 821.20(b) and the devices that FDA has designated for tracking at 21 CFR § 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993)).

If you have questions concerning this approval order, please contact Lisa Kennell at (301) 443-8262 extension 166.

Sincerely yours,

Susan Alpert, Ph.D., M.D
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

Issued: 5-2-95

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. **This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.**

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

   (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

   (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

  (a) has not been addressed by the device's labeling or

  (b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

(1) may have caused or contributed to a death or serious injury or

(2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Room 240
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

SUMMARY of SAFETY and EFFECTIVENESS DATA

Alliance Medical Technologies Inc.

MONOSTRUT™ Cardiac Prosthesis

Table of Contents

SUMMARY of SAFETY and EFFECTIVENESS DATA

Alliance Medical Technologies Inc.

MONOSTRUT™ Cardiac Prosthesis

1. General Information

Device Generic Name: .... Replacement Heart Valve

Device Trade Name: .... Monostrut™ Cardiac Valve Prosthesis

Applicant's Name and Address:..................... Alliance Medical Technologies, Inc.
17590 Gillette Avenue
Irvine, CA 92614

PMA Application Number: P970002

Date of Panel Recommendation:.................. September 15, 1997

Date of Notice of Approval to the Applicant: ..September 30, 1997

2. Indications For Use

The Monostrut™ Cardiac Prosthesis is indicated for the replacement of malfunctioning native or prosthetic aortic or mitral heart valve. Limited clinical data are available on large sizes.

3. Device Description

The Monostrut™ Cardiac Prosthesis is a hingeless tilting disc heart valve. It is constructed of an L605 cobalt-base alloy (e.g., Haynes 25) orifice ring with integral struts, and a pyrolytic carbon disc occluder with an encapsulated radiopaque marker. The prosthesis is provided with a PTFE fabric suture ring. The nominal opening angle of the prosthesis is 70°, with the disc free to rotate during operation.

The prosthesis is packaged in a rigid Double Aseptic Transfer (DAT) Package, which allows presentation of the complete inner container and prosthesis to the sterile field in an aseptic manner.

The Monostrut™ Cardiac Prosthesis is available in tissue annulus diameters sizes 21 to 33 mm for the aortic position and 27 to 33 mm diameters for the mitral position.

4. Contraindications

The Monostrut™ Cardiac Prosthesis is contraindicated in patients unable to tolerate anticoagulation therapy.

5. Warnings and Precautions

- **FOR SINGLE USE ONLY**
- **Avoid damaging the prosthesis**. Do not attempt to change the position of the struts or to remove the disc. The prosthesis must be handled only with a Monostrut™ Cardiac Prosthesis Holder Set, as damage may result in occluder escape or fracture with subsequent patient injury.
- **Do not pass a catheter through a Monostrut™ Cardiac Prosthesis** as this maneuver may cause valvular insufficiency or disc dislodgment or catheter entrapment.

5.1 Precautions Prior to use

Do not use the Monostrut™ Cardiac Prosthesis:

- if the prosthesis has been damaged.

Do not use the Monostrut™ Cardiac Prosthesis without resterilization:

- if the tamper evident seal is broken; or
- if the expiration date has elapsed.

5.2 Sterilization

- Do not use radiation sterilization techniques as these techniques will cause sewing ring degradation.
- Do not resterilize the prosthesis in the double aseptic transfer package.
- Do not resterilize after contact with body fluids.
- Do not resterilize more that 10 times (see section 11.6 Sterilization).

5.3 Precautions During Use

- Use only the Monostrut™ Cardiac Prosthesis Sizers to select the proper valve size as other sizers may result in improper valve selection. When seating the valve, ensure that neither suture material nor anatomic structures interfere with leaflet motion.[2]

- Avoid contact with or handling by metal or other abrasive instruments as they may scratch the highly polished prosthesis surfaces or bend the struts, which may cause dislodgment of the disc or provide a nidus for thrombus formation. Use rubber shod instrument for testing leaflet excursion.
- Avoid obstruction of the coronary ostia by the aortic valve sewing ring.

6. Alternative Practices and Procedures

Alternative procedures include medical therapy with drugs, and surgical treatments such as annuloplasty or valvuloplasty with or without the use of implantable materials (i.e., annuloplasty rings, sutures). When the patient requires replacement of his/her native or previously placed prosthetic valve, the option of choosing a mechanical or biological valve exists. The choice of replacement valve depends upon factors which include the patient's age, preoperative conditions, anatomy and ability to tolerate long term anticoagulation therapy.

Other forms of treatment may include the use of cardiac drug therapy.

7. Marketing History

There are more than 120,654 valves distributed (sizes 17-33 mm, aortic and mitral) to 34 countries from introduction in April 15, 1982 through June 30, 1997. Table 1 summarizes the complaints received for the Monostrut™ valve.

Table 7.1: Worldwide Complaints

Complaints	N	%
Disc Impingement	58	0.05%
Disc Fracture	9	0.01%
Suture Ring Rotation	10	0.01%
Suture Ring Separation	8	0.01%
Literature	4	<0.01%
Packaging	10	0.01%
User Problems	5	<0.01%
Cosmetic Flaw	1	<0.01%
Non-Valve Related	23	0.02%
Anticoagulant Bleeding	39	0.03%
Endocarditis	19	0.02%
Graft Valves	10	0.01%
Hemolysis	7	0.01%
Perivalvular Leak	34	0.03%
Sudden Death	11	0.01%
Thromboembolism	63	0.05%
Unacceptable hemodynamics	3	<0.01%
Valve Thrombosis	10	<0.01%
Total	324	0.27%

The Monostrut™ has not been withdrawn from the market in any country for any reason.

8. Adverse Events

Adverse events potentially associated with the use of prosthetic heart valves (in alphabetical order) include:

- cardiac arrhythmias
- death
- disc impingement (entrapment)
- endocarditis
- hemolysis
- hemorrhage, anticoagulation -related
- leak, transvalvular or perivalvular
- nonstructural dysfunction (inappropriate sizing, or other);
- prosthesis thrombosis

- structural deterioration
- valve thromboembolism

Events experienced by the patients in this study are summarized under Section 10.4 (Results).

9. Summaries of Nonclinical Studies

9.1 Bench Testing

Since 1972 over 60 publications have been issued on the hemodynamics, fatigue, strength, biocompatibility and clinical performance of the Monostrut™ heart valve or components. The two most recent peer review publications with clinical data are Liem[1] and Aris[2]. Some of these articles were used to provide comparison information.

9.1.1 Biocompatibility

The materials used in the Monostrut™ heart valve have a long history of use in cardiovascular applications. All of the blood contacting component materials (pyrolytic carbon occluder, expanded polytetrafluoroethylene sewing ring, polyethylene terephthalate sutures, and Haynes alloy flange) have been used in prosthetic heart valves approved for sale in the United States.

Selected short term tests recommended for Tripartite Biocompatibility Guidance For Medical Devices Document and to USP standards have been conducted on the materials used in the Monostrut™ heart valve. It was determined that long term toxicity tests were not required on materials due to the fact that the materials have all been used on prosthetic heart valves marketed in the United States.

Acceptable results were obtained from all biocompatibility tests conducted on selected materials. These test results, the data from *in vivo* experience in animals and humans, plus the extensive use of these materials in cardiovascular applications support the biocompatibility of materials used in the Monostrut™ heart valve.

9.1.2 Hydrodynamic Performance

Tests were conducted to measure the steady state flow pressure drop and effective orifice area across the Monostrut™ valve. Testing was conducted in horizontal straight mitral and aortic flow chambers at various flow rates. The test fluid used was a water/glycerol mixture with a viscosity of 3.05 cP and a density of 1.10 g/ml at room temperature. Size 21 mm and 29 mm commercially available valves were used as reference valves in the aortic position. A size 29 mm commercially available valve was used as a reference valve in the mitral position. Three of each size Monostrut™ valves were tested at flow rates ranging from 5-30 liters per minute (LPM). For Monostrut™ valves in the aortic position mean pressure drops ranged from 0.5 mmHg for the size 29 mm valve at 5 LPM to 62.7 mmHg for the size 19 mm valve at 25 LPM. In the mitral position mean pressure drops ranged from 0.5 mmHg for both the size 27 mm and 29 mm valve at 5 LPM to 62.3 mmHg for the size 19 mm valve at 25 LPM. Data for the Monostrut™ were comparable to the reference valves.

Tests were conducted to measure the pressure drop and effective orifice area across the Monostrut™ valve. Testing was conducted in a pulse duplicator. The test fluid used was a saline/glycerol mixture with a viscosity of 3.05 cP and a density of 1.10 g/ml at room temperature. The pulse duplicator simulated both aortic and mitral flow conditions and was instrumented to measure systolic and diastolic flow rates, volume flow rates (cardiac output), regurgitation and transvalvular pressures. A size 21 mm commercially available valve was used as a reference valve in the aortic position. A size 29 mm commercially available valve was used as a reference valve in the mitral position. Three of each size Monostrut™ valves were tested. Pressure drops were measured at cardiac outputs ranging from 2 to 8 LPM at 72 BPM. For Monostrut™ valves in the aortic position mean pressure drops ranged from 1.8 mmHg for the size 25 mm valve at 2 LPM to 144.6 mmHg for the size 17 mm valve at 8 LPM. In the mitral position mean pressure drops ranged from 1.0 mmHg for the size 27 mm valve at 2 LPM to 52.7 mmHg for the size 17 mm valve at 8 LPM. Data for the Monostrut™ valves were comparable to the reference valves. Over the range of flow tested the results are consistent with clinical requirements. Effective Orifice Area (EOA) values in the aortic position ranged from 0.7 cm^2 for the size 17 mm valve to 3.1 cm^2 for the size 29 mm valve. EOA values in the mitral position ranged from 0.7 cm^2 for the size 17 mm valve to 2.5 cm^2 for the 29 mm valve.

Tests were conducted to measure the proportion of back flow (regurgitation) through the Monostrut™ valve under pulsatile flow conditions in the normal physiological range. Testing was conducted in a pulse duplicator. The test fluid used was a physiological saline/glycerol mixture with a viscosity of 3.05 cP and a density of 1.10 g/ml at room temperature. Regurgitation was measured as a percentage of forward flow. A size 21 mm commercially available valve was used as a reference valve in the aortic position. A size 29 mm commercially available valve was used as a reference valve in the mitral position. Three of each size Monostrut™ valves were tested. Measurements were taken at cardiac outputs ranging from 2 to 8 LPM at pulse rates of 45, 72 and 120 BPM. For the Monostrut™ valve in the aortic position mean regurgitation percentages range from 0.8% for the size 19 mm valve at 45 BPM and 6 LPM to 28.9% for the size 29 mm valve at 120 BPM and 2 LPM. In the mitral position mean regurgitation percentages range from 1.3% for the size 17 mm valve at 45 BPM and 6 LPM to 37.4% for the size 29 mm valve at 120 BPM and 2 LPM. Larger Monostrut™ valves exhibited higher regurgitation percentages due to a greater sweep volume (during closing) by the larger diameter occluders.

Tests were conducted to measure back flow through a size 29 mm Monostrut™ valve at high pulse rates in the normal physiological range in the mitral position. A size 29 mm commercially available valve was used as a control valve. The test fluid used was physiological saline/glycerol mixture with a viscosity of 3.05 cP and a density of 1.10 g/ml at room temperature. Regurgitation data were taken at pulse rates of 100, 120, 160 and 190 BPM for three size 29 mm Monostrut™ valves. Diastolic mean RMS flow rates ranged from approximately 12 to 16.5 LPM. Regurgitation ratios ranged from a high of 28.4% to a low of 10.2%. The percentage of closing volume peaked at 78% for the Monostrut™ valve. This value is comparable to the commercially available value of 75% closing volume. Both valves were tested at 160 BPM.

Testing was conducted to measure the leakage volumes of the Monostrut™ at dynamic back pressures. Measurements were taken at four values for mean ventricular and aortic pressures (40, 60, 80 and 100 mmHg; and 80, 100, 120 and 160 mmHg, respectively). Three Monostrut™

valves of each size were tested in both the aortic and mitral positions. The test fluid used was a physiological saline/glycerol mixture with a viscosity of 3.05 cP and a density of 1.10 g/ml at room temperature. Reference valves included a 21 mm commercially available valve tested in the aortic position, and one size 29 mm commercially available valve tested in the mitral position. The largest mean leakage volumes for the Monostrut™ valve were 3.6 ml for the size 29 mm valve at a mean aortic pressure of 120 mmHg, and 3.5 ml for the size 23 mm valve at a mean ventricular pressure of 100 mmHg. Leakage volumes for the Monostrut™ valve are comparable and generally less than the reference valves.

Two separate studies were conducted by consultants for the purpose of evaluating velocity fields at pulsatile flow. The Monostrut™ was compared to valves which have been on the market.

In one study, the Monostrut™ was compared to the predecessor models to the Monostrut™. The consultant concluded that the laminar shear stress values and possible blood damage are acceptable and below those quoted in the literature as the critical threshold, and that no backflow was observed, which may result in decreased stagnation area.

In the other study, velocities and shear stresses were measured and presented for the size 27 mm Monostrut™. Peak shear stresses were measured at 1500 dynes/cm^2. Mean shear stresses ranged from 100 to 750 dynes/cm^2. Overall, the Monostrut™ was found hemodynamically comparable to two commercially available mechanical valves.

9.1.3 Structural Performance

Testing was conducted to determine the static pressure required to permanently deform and/or fracture the occluder or strut of the size 29 mm Monostrut™ valve. The test fluid used was deionized water. Testing was conducted in two separate parts. The first part of the test subjected the valves to hydrostatic pressure until plastic deformation of 0.0001 inch was detected while hard mounted. A mean pressure of 44.7 psi was required to plastically deform the valve. The second part of the test was identical to the first with the exception of mounting techniques. In the second part the valves were mounted with suture rings. The valves experienced pressure to approximately 130 psi (maximum equipment capacity) without failure.

Each strut for eleven size 29 mm Monostrut™ valves was statically loaded in directions parallel to the physiological direction of flow and the yield load determined. All struts were polished to within 0.005 inch of minimum requirements at the base of the struts. Average yield loads of 5.4 and 6.8 Kg were determined for the size 29 mm Monostrut™ inlet and outlet strut, respectively.

Testing was conducted to measure the peak physiological impact loads on both the inlet and outlet struts. Three size 17, 23 and 29 mm Monostrut™ valves in nominal tolerance were tested in both the aortic and mitral positions. Two size 29 mm Monostrut™ valves with marginal and out-of-tolerance attributes were tested in both the aortic and mitral positions. All valves were tested at peak systolic pressures of 120 and 200 mmHg and pulse rates of 72 and 120 BPM corresponding to normal and elevated physiological conditions, respectively.

The highest measured loads were found in the size 29 mm valve. Under normal physiological conditions with marginal attributes, the mean peak physiological loads were 1188 and 142 grams for the inlet and outlet struts, respectively. Under elevated physiological conditions with marginal attributes, the mean peak physiological loads were 2246 and 240 grams for the inlet and outlet struts, respectively.

Testing was conducted to determine the time of peak disc impact relative to the cardiac cycle on the inlet and outlet strut of a size 29 mm Monostrut™ valve with a suture ring. The valve was evaluated in the aortic and mitral positions at normal and elevated physiological conditions. Peak opening and closing impact times were measured relative to the cardiac cycle. Mean systolic durations of approximately 35% were used. Test fluid was a physiological saline/glycerol solution. Mitral and aortic opening impact times ranged from 3.2 ms before to 12.5 ms after Isovolumetric Expansion (IVE) end and 6.9 ms before to 5.5 ms after Isovolumetric Contraction (IVC) end, respectively. Mitral and aortic closing impact times ranged from 3.2 to 3.4 ms before IVC start and 17.7 to 22.2 ms after IVE start, respectively.

Testing was conducted on the inlet and outlet struts of the size 29 mm Monostrut™ valve to determine the creep of the struts after 200 cycles at high loads. A zero to maximum load parallel to the direction of physiological flow was applied 200 times to the strut being tested. The value for creep was determined by comparing the difference between the initial and final positions of the struts to an accuracy of 0.0005" and 0.0001" for the inlet and outlet struts, respectively. After 200 cycles, there was no difference in initial and final deflections.

Fatigue testing was conducted to empirically measure the fatigue endurance characteristics of the inlet and outlet struts of the size 29 mm Monostrut™ valve. Seven outlet and eight inlet struts were tested at 50 to 110 Hz in a test apparatus which applied a non-reversed, zero to maximum cyclic load in the direction of physiological flow. Testing was conducted in room air. Struts were fatigued to approximately 400 million cycles or until failure and then subjected to an additional approximately 200 million cycles. The S-N plot reveals no failure at loads of 6000 gm or less for the inlet strut and no failure at loads of 4000 gm or less for the outlet strut.

In addition to an S-N analysis, fracture mechanics-based damage-tolerant analyses were conducted at peak loads for both normal and elevated physiological conditions. These analyses were conducted for the size 17, 23 and 29 mm Monostrut™ valves. The S-N analysis revealed stresses at the base of either strut under worst case elevated physiological conditions indicating that in all cases the peak in-service stresses remain a factor of 2 to over 25 times smaller than the stresses to cause fatigue failure. Damage-tolerant analyses revealed acceptable fatigue life can be anticipated provided cracks are detected at 125 microns.

Three size 29 mm Monostrut™ valves and two size 29 mm commercially available valves were tested under conditions of elevated hydraulic pressures and accelerated cycling rates of 537 cycles per minute. The commercially available valves failed at 120,000 cycles and 140,000 cycles at 40 psi (2070 mm Hg) differential backpressure due to a disc escape and a fractured inlet strut. The Monostrut™ valves survived 500,000 cycles at 40 psi and an additional 500,000 cycles at 80 psi (4140 mmHg) without failing. Thus, no failures of the Monostrut™ valves occurred at a differential backpressure of 4140 mmHg which is over 34 times the normal physiological backpressure of 120 mmHg.

Three-dimensional linear finite elements analyses were performed to determine the maximum stresses in the struts of the size 17, 23 and 29 mm Monostrut™ valves during the disc insertion process and during valve opening and closing at both normal and elevated physiological conditions. The highest operating stresses were for the size 29 mm valve. At elevated physiological conditions maximum operating stresses were at 23.6 ksi for the inlet strut and 3.2 ksi for the outlet strut. The highest stresses during the disc insertion process occurred in the size 17 mm valves.

Uni-axial tensile testing was conducted to determine the tensile properties of L605. The yield stress at 2.0% offset was 66,500 psi. The ultimate tensile strength was 144,600 psi. The Elastic Modulus of the materials was 30.3×10^6. A series of low cycle fatigue tests were conducted on L605 to evaluate the effect of the disc insertion procedure on the fatigue life of the valve strut. It was found that the disc insertion uses much less than 1/18 of the fatigue life of the outlet strut.

Near threshold fatigue growth rate testing was conducted to determine crack propagation behavior of L605. Barstock material was machined into specimens and tested in air and lactated Ringer's solution. Threshold stress intensities ranged from 2.35 ksi-in$^{1/2}$ at a stress ratio of 0.75 to 9.62 ksi-in$^{1/2}$ at a stress ratio of 0.05.

Testing was conducted to examine the fatigue endurance characteristics of a size 29 mm Monostrut valve notched at the base of the inlet and outlet struts. Notches 0.020" deep were machined across the strut bases as crack initiators. The struts were placed in a test apparatus which applied a non-reversed, zero to maximum cyclic load in the direction of physiological flow at 50 and 100 Hz. After 400 million cycles no crack growth was noted.

Testing was conducted to determine wear patterns and the amount of wear on the inlet and outlet struts and disc after extended number of cycles at high cycle rates. The test apparatus was instrumented to cycle at 1075 BPM with opening pressures of 259 mmHg and closing backpressures of 75 mmHg. The test fluid used was deionized water at 37° C. Six size 29 mm Monostrut™ valves and three size 29 mm commercially available valves were concurrently tested to 10 equivalent years of cycling and then subjected to an additional 5 equivalent years of cycling. The maximum mean disc wear noted for the 29 mm Monostrut™ valve was 5.6 microns after 570 million cycles.

9.2 Animal Testing

The animal study was conducted in eight dogs which were considered to be in good health by the investigator. Sizes and quantities of valves implanted were as follows: size 21(1), size 23(6), size 25(1). All the dogs were maintained on sodium warfarin anticoagulation therapy.

In the six dogs which survived the post-operative period, hemodynamic evaluation of left ventricular pressure and pulmonary capillary wedge pressures were obtained in order to calculate the end-diastolic transprosthetic pressure gradients. Two of these six dogs presented with transprosthetic gradients of 12 mm Hg and 9 mm Hg, respectively. The remaining four dogs presented with no detectable transprosthetic gradients (0 mm Hg). The observed maximum disc opening angle for the Monostrut™ valve was 70°. Cineangiographic visualization showed a minor degree of valvular regurgitation. Hematology, assessing red blood cell counts, hemoglobin and hematocrit data showed no evidence of uncompensated anemia.

Mitral valve replacement in the canine using the Monostrut™ valve demonstrated adequate surgical handing characteristics, short term safety and hemodynamic performance.

9.3 Shelf life

Simulated valves were used to establish a five year shelf life. Sixty-three (60 test, 3 control) double aseptic transfer (DAT) packages were sterilized the maximum number of times. The DAT packages were then accelerated aged for five years and stressed in combination of extreme high and low temperature, and extreme high and low humidity. After completion of stressing, the packages were subjected to a rigorous simulated shipping test. Upon completion of all testing the packages were placed in a microbial challenge chamber. The units were tested for sterility after the microbial challenge and found to be sterile. The three controls were positive for growth. Testing has demonstrated that the package, when subjected to sterilization, shipping, aging of five years, and microbial challenge, will provide an effective barrier to maintain sterility of the Monostrut™ Heart Valve for five years.

9.4 Sterilization

Tests were conducted to evaluate the effect on multiple sterilization cycles on the sewing fabric. After undergoing multiple sterilization cycles, tensile testing was completed. The testing showed no significant degradation to the material after 5 years aging and ten times sterilization. In addition, the sewing ring was clamped into a test fixture to perform a pull off test. The loads required to remove the sewing ring from the valve were 29 to 55 lb. These loads are significantly higher than the in vivo loads experienced by the components. It was determined that repeated sterilization cycles of up to ten cycles did not compromise the physical integrity of the sewing ring materials or the sewing ring's functional integrity.

10. Summaries of Clinical Studies

10.1 Objectives

The objectives of the study were to assess safety of the valve by documenting adverse events using standardized definitions of complications, and to evaluate effectiveness by monitoring the New York Heart Association classification and hemodynamic performance (via catheterization).

10.2 Methods

Patients requiring isolated aortic or mitral heart valve replacement were enrolled from 1987 to 1992 at three Canadian centers. Hemodynamic (by catheterization), NYHA classification, and blood data were obtained preoperatively, at 3-6 months postoperative, and annually thereafter. Patients were monitored throughout the postoperative period for possible adverse events.

Patient anticoagulation was left to the discretion of the following physician. The antiplatelet and anticoagulant agents used were reported. Of the 269 patients at the two year follow-up, the majority (215) were receiving warfarin alone, five were receiving warfarin in combination, and one patient was receiving aspirin only.

The cohort included 314 patients (172 men, 142 women), aged from 23 to 85 years (mean of 56 years). Cumulative follow-up was 1391 patient-years with mean follow-up of 4.4 patient-years (SD=2.1 years, range = 0-8 years).

10.3 Description of Patients and Analysis for Gender Bias

Study inclusion and exclusion criteria were designed and the study carried out to avoid gender bias in patient enrollment. Of all patients enrolled, 172 of 314 (55%) were male. This proportion of males (172/142=1.21) is consistent with the male to female incidence of patients presenting for valve replacement in the US and Canada[3,4,5] (range 1.04 to 1.44).

Based on univariate analyses, there was no association between any of the complications with the exception of an association between gender and valve thrombosis (p=0.05), but the number of events was small. Only 6 females and one male had at least one valve thrombosis.

Table 7.1: Patient Characteristics

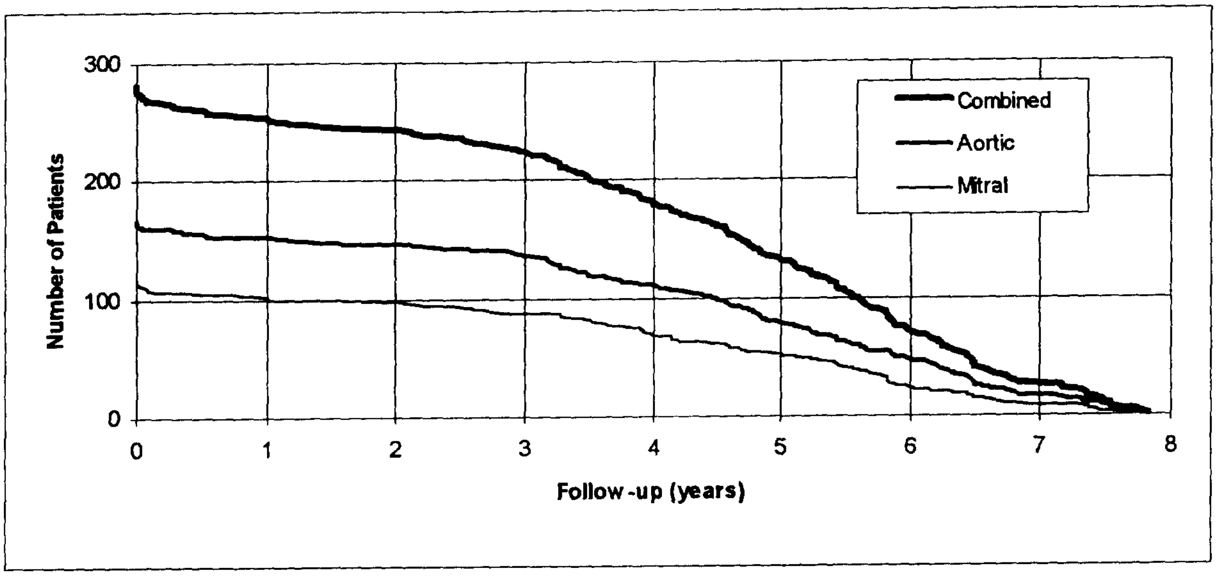
All patients implanted, N=314, 1391 patient years

Description of Patients	Aortic Valve (N=178)	Mitral Valve (N=136)
Age (mean ± SD, N [min., max.])	56±11, 178 [23, 77]	56±11, 136 [30, 84]
Gender (%male/% female)	72%/28%	32%/68%
Etiology of valve disease		
Regurgitation - % of pts. With significant regurgitation (% (number in subgroup/N))	16% (29/178)	18% (24/136)
Stenosis - % of pts. with any stenosis (% (number in subgroup/N))	31% (55/178)	25% (34/136)
Mixed - % of pts. with sign. Regurgitation and any stenosis (% (number in subgroup/N))	39% (69/178)	34% (46/136)

Figure 7.1 shows the number of patients implanted *versus* duration of follow-up in the graphic with a breakdown by valve location (aortic and mitral). Table 7.2 shows the number of patients implanted Table 7.3 shows the duration of follow-up for each valve size and implant location.

Figure 7.1: Number of Patients by Location over Time

All patients implanted, approved sizes, N=282



Year	0	1	2	3	4	5	6	7
Combined	**282**	**253**	**243**	**223**	**180**	**132**	**71**	**26**
Aortic	166	152	146	135	111	79	47	17
Mitral	116	101	97	88	69	53	24	9

Table 7.2: Number of Patients Implanted and Number with Hemodynamic Data

By Implant Location and Valve Size, All patients implanted, approved sizes, N=282

Implant location	**Valve size (mm)**					
	21	**23**	**25**	**27**	**29-33**	Total
Aortic	30/17	56/15	56/8	20/10	4/4	166/54
Mitral	-	-	-	41/13	75/17	116/30
Total	30/17	56/15	56/8	61/23	79/21	282/84

Table 7.3: Number of Patient-years by Implant Location and Valve Size

By Implant Location and Valve Size, All patients implanted, approved sizes, N=282

Implant location	**Valve size (mm)**					
	21	**23**	**25**	**27**	**29-33**	Total
Aortic	112.1	293.1	239.4	97.1	20.6	762
Mitral	-	-	-	179.4	318.7	498
Total	112	293	239	277	339	1260

10.4 Results

In Table 6.1, the observed adverse events for: 1) early events (occurring ≤ 30 days post-implant); 2) late events (occurring > 30 days post-implant); and 3) overall events are shown. Late events are expressed as an in the table are the linearized rates.

Table 6.1: Observed Adverse Events

	Early Events	Late Events	Actuarial Freedom by Kaplan-Meier	
	% of pts. (N)	%/ pt-yr. (N)	1 Year [95% CI]	5 Years [95% CI]
Aortic Valve Replacement, All patients implanted: N=178, Cumulative Follow-up=820 patient-years				
Death (all causes)	2.2% (4)	2.8% (23)	91.8% [87.7%-95.9%]	81.6% [71.7%-91.5%]
Death (valve-related/unexplained)	0.0% (0)	1.2% (10)	96.4% [93.5%-99.2%]	93.1% [86.1%-100%]
Thromboembolism	2.2% (4)	1.8% (15)	95.8% [92.7%-98.9%]	85.3% [75.6%-94.6%]
Permanent Neurological Events	1.7% (3)	1.0% (8)	97.6% [95.2%-100%]	90.7% [82.6%-98.7%]
Transient Neurological Events	0.6% (1)	0.9% (7)	98.2% [96.2%-100%]	92.5% [85.1%-99.9%]
Non-Neurological Events	0.0% (0)	0.0% (0)	100%	100%
Valvular Thrombosis	0.0% (0)	0.4% (3)	98.8% [97.0%-100%]	96.7% [91.6%-100%]
Structural Deterioration	0.0% (0)	0.0% (0)	100%	100%
Nonstructural Dysfunction	0.0% (0)	0.0% (0)	100%	100%
Anticoagulant-Related Hemorrhage	0.6% (1)	1.7% (14)	97.5% [95.1%-99.9%]	88.3% [78.9%-97.8%]
Perivalvular Leak	1.1% (2)	2.0% (16)	95.8% [92.7%-98.9%]	90.4% [82.2%-98.6%]
Endocarditis	1.1% (2)	0.7% (6)	98.2% [96.2%-100%]	90.5% [82.5%-98.6%]
Hemolysis	0.0% (0)	1.3% (11)	94.5% [90.9%-98.1%]	92.6% [87.2%-98.1%]
Reoperation	0.6% (1)	0.9% (7)	97.6% [95.3%-99.9%]	94.2% [87.6%-100%]
Explant	0.0% (0)	0.6% (5)	98.8% [97.1%-100%]	95.4% [89.6%-100%]

Mitral Valve Replacement, All patients implanted: N=136, Cumulative Follow-up=572 patient-years				
Death (all causes)	6.6% (9)	2.6% (15)	90.5% [85.4%-95.6%]	77.2% [63.5%-90.9%]
Death (valve-related/unexplained)	0.7% (1)	1.4% (8)	97.6% [94.8%-100%]	89.9% [79.4%-100%]
Thromboembolism	2.2% (3)	4.4% (25)	94.2% [90.0%-98.5%]	72.9% [61.7%-84.1%]
Permanent Neurological Events	1.5% (2)	1.9% (11)	96.8% [93.6%-99.9%]	84.5% [72.0%-97.1%]
Transient Neurological Events	0.7% (1)	2.5% (14)	97.5% [94.6%-100%]	85.8% [76.8%-94.7%]
Non-Neurological Events	0.0% (0)	0.0% (0)	100%	100%
Valvular Thrombosis	0.0% (0)	0.7% (4)	99.1% [97.4%-100%]	98.2% [95.8%-100%]
Structural Deterioration	0.0% (0)	0.0% (0)	100%	100%
Nonstructural Dysfunction	0.7% (1)	0.3% (2)	99.2% [97.6%-100%]	99.2% [97.6%-100%]
Anticoagulant-Related Hemorrhage	2.9% (4)	1.7% (10)	94.2% [90.0%-98.4%]	86.4% [73.3%-99.4%]
Perivalvular Leak	2.9% (4)	1.7% (10)	94.3% [90.1%-98.5%]	82.8% [69.3%-96.3%]
Endocarditis	0.0% (0)	0.3% (2)	100%	98.2% [95.8%-100%]
Hemolysis	0.0% (0)	0.5% (3)	98.3% [96.0%-100%]	96.6% [92.0%-100%]
Reoperation	5.1% (7)	1.4% (8)	90.3% [85.1%-95.6%]	88.2% [81.5%-95.0%]
Explant	2.2% (3)	1.0% (6)	95.1% [91.3%-99.0%]	93.0% [87.6%-98.4%]

The relatively high thromboembolism rate and relatively low rate of major bleeding observed in the clinical study are consistent with a low level of patient anticoagulation.

Table 7.4: Effectiveness Outcomes

All patients catheterized[1]: N = 96, all values reported as: number in subgroup/N, mean ± SD (min, max.)

Endpoint	Pre-op	Early[2]	Late[3]	Annual
Aortic Valve Replacement All patients implanted: N = 314, all values reported as: number in subgroup/N, mean ± SD (min, max.)				
Functional NYHA	61/61, 3.1 ± 0.7 (2 - 4)	14/61, 1.9 ± 0.9 (1 - 4)	29/61, 1.2 ± 0.4 (1 - 2)	35/61, 1.4 ± 0.6 (1 - 2)
Valvular Regurgitation	–	3/61, 1.3 ± 0.5 (1 - 2)	23/61, 1.1 ± 0.3 (1 - 2)	35/61, 1.1 ± 0.3 (0 - 2)
Valve Gradient[4] (mm Hg)				
21mm	–	–	6/61, 12.8 ± 9.7 [0,30]	11/61, 11 ± 3.4 [5,17]
23mm	–	–	4/61, 7.4 ± 3.7 [3,12]	11/61, 9.8 ± 4.0 [3,20]
25mm	–	1/61, 12 ± 0 [n/a]	2/61, 2.5 ± 2.5 [0,5]	5/61, 9.2 ± 2.1 [5,11]
27mm	–	–	5/61, 3.8 ± 3.2 [0,7]	4/61, 7.5 ± 4.3 [0,10]
29mm	–	–	3/61, 3.1 ± 2.6 [0,6.4]	1/61, 6 ± 0 [n/a]
Effective Orifice Area (mm^2)				
21mm	–	–	6/61, 1.5 ± 0.4 [1.1,2.3]	11/61, 1.4 ± 0.2 [1,1.7]
23mm	–	–	4/61, 1.4 ± 0.9 [0.6,3]	11/61, 1.8 ± 0.4 [1.2,2.2]
25mm	–	1/61, 2.3 ± 0 [n/a]	2/61, 2.5 ± 0.2 [2.3,2.7]	5/61, 2.1 ± 0.4 [1.5,2.6]
27mm	–	–	5/61, 2.4 ± 0.8 [1.4,3.9]	4/61, 2.4 ± 0.4 [2,2.8]
29mm	–	–	3/61, 2.2 ± 0.2 [2,2.4]	1/61, 3.5 ± 0 [n/a]
Mitral Valve Replacement				
Functional NYHA	34/35, 3.0 ± 0.5 (1 - 4)	9/35, 2.6 ± 0.8 (1 - 4)	18/35, 1.4 ± 0.6 (1 - 4)	16/35, 1.7 ± 0.8 (1 - 4)
Valvular Regurgitation	–	9/35, 1.3 ± 1.1 (0 - 3)	11/35, 1.1 ± 0.5 (0 - 2)	15/35 1.6 ± 1.1 (1 - 4)
Mean Gradient (mm Hg)				
27mm	–	2/35, 7.1 ± 0.1 [7,7.2]	6/35, 6.3 ± 1.2 [5,8.3]	5/35, 5.4 ± 2.5 [2.7,8.4]
29mm	–	3/35, 2.0 ± 1.4 [0,3]	3/35, 6.3 ± 0.5 [6,7]	5/35, 5.5 ± 6.3 [1.4,18.1]
31mm	–	2/35, 4.6 ± 0.5 [4.1,5]	2/35, 4.5 ± 3.5 [1,8]	3/35, 3.8 ± 1.1 [2.3,5]
33mm	–	–	–	1/35, 12 ± 0 [n/a]
Effective Orifice Area (mm^2)				
27mm	–	2/35, 1.5 ± 0.1 [1.4,1.5]	6/35, 1.9 ± 0.7 [1.2,3.2]	5/35, 2.2 ± 0.7 [1.4,3.3]
29mm	–	2/35, 2.6 ± 0.1 [2.5,2.7]	3/35, 1.6 ± 0.1[1.5,1.7]	5/35, 2.1 ± 0.7 [0.8,2.7]
31mm	–	2/35, 2.6 ± 0.6 [2,3.1]	2/35, 2.4 ± 0.6 [1.8,3]	3/35, 3.3 ± 1.1 [1.9,4.7]

1. *Catheterization data was collected on 96 patients (61 aortic, 35 mitral). The majority of these patients (92) came from 7 centers not enrolled in this study*
2. *Early post-operative evaluation conducted at 30-days post-implantation or hospital discharge.*
3. *Late post-operative evaluation conducted at 3-6 months post-implantation.*
4. *The "peak-to-peak" difference between systolic pressure measurements obtained just proximal and distal to a semilunar valve. The mean gradient is used to denote the gradient across an atrioventricular valve.*

11. Risk-Benefit Analysis

Laboratory and clinical data provide reasonable assurance that the Monostrut™ Cardiac Prosthesis is safe and effective when used according to the approved labeling.

12. Conclusions Drawn from Studies

The laboratory and engineering studies performed on MONOSTRUT™ Cardiac Prosthesis demonstrate that the device is made of biocompatible materials, has acceptable hydrostatic performance under static and pulsatile flow conditions compared to a control, has acceptable structural performance (fatigue and wear of the strut and occluder) under physiological and elevated physiological conditions compared to a control valve.

The laboratory testing performed on the device suggest that this device is suitable for long-term implant. The MONOSTRUT™ Cardiac Prosthesis meets specifications for performance and is comparable to existing approved heart valves.

The animal studies show that the MONOSTRUT™ Cardiac Prosthesis demonstrated acceptable hemodynamic and handling performance *in vivo* .

The clinical studies submitted in the PMA provide scientific evidence that the MONOSTRUT™ Cardiac Prosthesis is safe and effective in providing acceptable hemodynamic performance as demonstrated in the improvement in the NYHA classification postoperatively, and in the catheterization data. There was some evidence of hemolysis with this valve, demonstrated by the elevated levels of lactate dehydrogenase and decrease in haptoglobin over time post implant. Acute and long-term complication rates were comparable to those reported in the literature for most types of complications. Rates for perivalvular leak and thromboembolism in mitral valve recipients were slightly higher than historically reported rates.

13. Panel Recommendations

On September 15, 1997, the Circulatory System Devices Panel reviewed the data submitted by Alliance Medical Technologies, Inc. in support of marketing approval for Monostrut™ Cardiac Prosthesis for use for the replacement of malfunctioning native or prosthetic aortic or mitral heart valve in patients who can tolerate anticoagulation.

The panel recommended that certain sizes of the valve (sizes 21 mm and greater in the aortic model, and sizes 27 mm and greater in the mitral model) be approved. The small sizes (sizes 17 and 19 mm in the aortic model, and sizes 17, 19, 21, 23, and 25 mm in the mitral model) were not approved. There were conditions placed on the sponsor for a post approval clinical study to determine the long-term performance, and for some refinements to the labeling.

14. FDA Decision

The FDA agreed with the Panel's decision. Alliance Medical Technologies, Inc. submitted amendments to the PMA which satisfactorily addressed the remaining concerns of the FDA and the Panel. FDA issued an approval order on September 30, 1997. The applicant's manufacturing facility was inspected and was found to be in compliance with the device Good Manufacturing Practice regulations (21 CFR Part 820).

15. Approval Specifications

Directions for use: See the labeling.

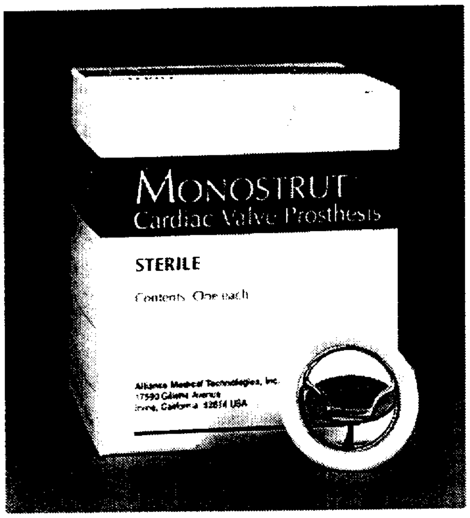
Hazards to health from use of the device: See indications, contraindications, warnings, precautions and adverse events in the labeling.

Postapproval requirements and restrictions: See approval order.

16. References

1. Liem K et al: The Monostrut prosthetic valve-predictors for valve related events during an eight years' Experience. Journal of Cardiovascular Surgery 1993; 35 (5):
2. Aris A: The Spanish Monostrut Study Group: A Ten-Year Experience With 8,599 Implants. Annuals of Thoracic Surgery 1996; 62:40-7
3. Akins CW. Long term results with the Medtronic Hall valvular prosthesis. Annals of Thoracic Surgery 1996;61:806-13.
4. Copeland JG er al. Four year experience with the CarboMedics valve: the North American experience. Annals of Thoracic Surgery 1994;58:630-7.
5. Fernandez J et al. Early and late-phase events after valve replacement with the St. Jude Medical prosthesis in 1200 patients. Journal of Thoracic Cardiovascular Surgery 1994;107:394-407.

MONOSTRUT™ CARDIAC PROSTHESIS



MONOSTRUT™ Cardiac Prosthesis

INSTRUCTIONS FOR USE

Contents

CAUTION: Federal law (U.S.A.) restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

1.DEVICE DESCRIPTION

The Monostrut™ Cardiac Prosthesis is a hingeless tilting disc heart valve. It is constructed of an L605 cobalt-base alloy (e.g., Haynes 25) orifice ring with integral struts, and a pyrolytic carbon disc occluder with an encapsulated radiopaque marker. The prosthesis is provided with a PTFE fabric suture ring. The nominal opening angle of the prosthesis is 70°, with the disc free to rotate during operation.

The prosthesis is packaged in a rigid Double Aseptic Transfer (DAT) Package, which allows presentation of the complete inner container and prosthesis to the sterile field in an aseptic manner. The Monostrut™ Cardiac Prosthesis is available in tissue annulus diameter sizes 21 to 33 mm for the aortic position and 27 to 33 mm diameters for the mitral position.

2. INDICATIONS

The Monostrut™ Cardiac Prosthesis is indicated for the replacement of malfunctioning native or prosthetic aortic or mitral heart valve.[1] Limited clinical data are available on large sizes (see CLINICAL STUDIES).

3. CONTRAINDICATIONS

The Monostrut™ Cardiac Prosthesis is contraindicated in patients unable to tolerate anticoagulation therapy.[2]

4. WARNINGS

- **FOR SINGLE USE ONLY**
- **Avoid damaging the prosthesis.** Do not attempt to change the position of the struts or to remove the disc. The prosthesis must be handled only with a Monostrut™ Cardiac Prosthesis Holder Set, as damage may result in occluder escape or fracture with subsequent patient injury.
- **Do not pass a catheter through a Monostrut™ Cardiac Prosthesis** as this maneuver may cause valvular insufficiency or disc dislodgment or catheter entrapment.

5. PRECAUTIONS

5.1 Precautions Prior to Use

Do not use the Monostrut™ Cardiac Prosthesis:

- if the prosthesis has been damaged.

Do not use the Monostrut™ Cardiac Prosthesis without resterilization:

- if the tamper evident seal is broken; or
- if the expiration date has elapsed.

5.2 *Sterilization*

- Do not use radiation sterilization techniques as these techniques will cause sewing ring degradation.
- Do not resterilize the prosthesis in the double aseptic transfer package.
- Do not resterilize after contact with body fluids.
- Do not resterilize more that 10 times (see Section 11.6 Sterilization).

5.3 *Precautions During Use*

- Use only the Monostrut™ Cardiac Prosthesis Sizers to select the proper valve size as other sizers may result in improper valve selection. When seating the valve, ensure that neither suture material nor anatomic structures interfere with disc motion.[3]
- Avoid contact with or handling by metal or other abrasive instruments as they may scratch the highly polished prosthesis surfaces or bend the struts, which may cause dislodgment of the disc or provide a nidus for thrombus formation. Use rubber shod instrument for testing leaflet excursion.
- Avoid obstruction of the coronary ostia by the aortic valve sewing ring.

6. ADVERSE EVENTS

A total of 314 Monostrut™ Cardiac Prostheses were implanted in 314 patients at 3 centers. The mean follow-up was 4.4 years (range 1 month to 8 years) with a total of 1391 patient years.

A total of 51 deaths occurred during the study. Nineteen of these were judged by a committee to be related to the prosthesis. The reasons for deaths were endocarditis (5 patients), paravalvular leak (2 patients), valve thrombosis (3 patients), CVA (2 patients), and unknown in 7 patients.

6.1 *Observed Adverse Events*

In Table 6.1, the observed adverse events for: 1) early events (occurring ≤ 30 days post-market); 2) late events (occurring > 30 days post-implant); and 3) overall events are shown. Late events are expressed as linearized rates.

Table 6.1: Observed Adverse Events

	Early Events	Late Events	Actuarial Freedom by Kaplan-Meier	
	% of pts. (N)	%/ pt-yr. (N)	1 Year [95% CI]	5 Years [95% CI]
Aortic Valve Replacement, All patients implanted: N=178, Cumulative Follow-up=820 patient-years				
Death (all causes)	2.2% (4)	2.8% (23)	91.8% [87.7%-95.9%]	81.6% [71.7%-91.5%]
Death (valve-related/unexplained)	0.0% (0)	1.2% (10)	96.4% [93.5%-99.2%]	93.1% [86.1%-100%]
Thromboembolism	2.2% (4)	1.8% (15)	95.8% [92.7%-98.9%]	85.3% [75.6%-94.6%]
Permanent Neurological Events	1.7% (3)	1.0% (8)	97.6% [95.2%-100%]	90.7% [82.6%-98.7%]
Transient Neurological Events	0.6% (1)	0.9% (7)	98.2% [96.2%-100%]	92.5% [85.1%-99.9%]
Non-Neurological Events	0.0% (0)	0.0% (0)	100%	100%
Valvular Thrombosis	0.0% (0)	0.4% (3)	98.8% [97.0%-100%]	96.7% [91.6%-100%]
Structural Deterioration	0.0% (0)	0.0% (0)	100%	100%
Nonstructural Dysfunction	0.0% (0)	0.0% (0)	100%	100%
Anticoagulant-Related Hemorrhage	0.6% (1)	1.7% (14)	97.5% [95.1%-99.9%]	88.3% [78.9%-97.8%]
Paravalvular Leak	1.1% (2)	2.0% (16)	95.8% [92.7%-98.9%]	90.4% [82.2%-98.6%]
Endocarditis	1.1% (2)	0.7% (6)	98.2% [96.2%-100%]	90.5% [82.5%-98.6%]
Hemolysis	0.0% (0)	1.3% (11)	94.5% [90.9%-98.1%]	92.6% [87.2%-98.1%]
Reoperation	0.6% (1)	0.9% (7)	97.6% [95.3%-99.9%]	94.2% [87.6%-100%]
Explant	0.0% (0)	0.6% (5)	98.8% [97.1%-100%]	95.4% [89.6%-100%]
Mitral Valve Replacement, All patients implanted: N=136, Cumulative Follow-up=572 patient-years				
Death (all causes)	6.6% (9)	2.6% (15)	90.5% [85.4%-95.6%]	77.2% [63.5%-90.9%]
Death (valve-related/unexplained)	0.7% (1)	1.4% (8)	97.6% [94.8%-100%]	89.9% [79.4%-100%]
Thromboembolism	2.2% (3)	4.4% (25)	94.2% [90.0%-98.5%]	72.9% [61.7%-84.1%]
Permanent Neurological Events	1.5% (2)	1.9% (11)	96.8% [93.6%-99.9%]	84.5% [72.0%-97.1%]
Transient Neurological Events	0.7% (1)	2.5% (14)	97.5% [94.6%-100%]	85.8% [76.8%-94.7%]
Non-Neurological Events	0.0% (0)	0.0% (0)	100%	100%
Valvular Thrombosis	0.0% (0)	0.7% (4)	99.1% [97.4%-100%]	98.2% [95.8%-100%]
Structural Deterioration	0.0% (0)	0.0% (0)	100%	100%
Nonstructural Dysfunction	0.7% (1)	0.3% (2)	99.2% [97.6%-100%]	99.2% [97.6%-100%]
Anticoagulant-Related Hemorrhage	2.9% (4)	1.7% (10)	94.2% [90.0%-98.4%]	86.4% [73.3%-99.4%]
Perivalvular Leak	2.9% (4)	1.7% (10)	94.3% [90.1%-98.5%]	82.8% [69.3%-96.3%]
Endocarditis	0.0% (0)	0.3% (2)	100%	98.2% [95.8%-100%]
Hemolysis	0.0% (0)	0.5% (3)	98.3% [96.0%-100%]	96.6% [92.0%-100%]
Reoperation	5.1% (7)	1.4% (8)	90.3% [85.1%-95.6%]	88.2% [81.5%-95.0%]
Explant	2.2% (3)	1.0% (6)	95.1% [91.3%-99.0%]	93.0% [87.6%-98.4%]

The relatively high thromboembolism rate and relatively low rate of major bleeding rates observed in the clinical study are consistent with a low level of patient anticoagulation.

6.2 *Potential Adverse Events*

Adverse events potentially associated with the use of prosthetic heart valves (in alphabetical order) include:

- cardiac arrhythmias
- death
- disc impingement (entrapment)
- endocarditis
- hemolysis
- hemorrhage, anticoagulation related
- leak, transvalvular or parivalvular
- nonstructural dysfunction (inappropriate sizing, or other);
- prosthesis thrombosis
- structural deterioration
- valve thromboembolism

7. CLINICAL STUDIES

Patients requiring isolated aortic or mitral heart valve replacement were enrolled from 1987 to 1992 at three Canadian centers. Hemodynamic (by catheterization), NYHA classification, and blood data were obtained preoperatively, at 3-6 months postoperative, and annually thereafter. Patients were monitored throughout the postoperative period for possible adverse events.

Patient anticoagulation was left to the discretion of the following physician. The antiplatelet and anticoagulant agents used were reported. Of the 269 patients at the two year follow-up, the majority (215) were receiving warfarin alone, five were receiving warfarin in combination, and one patient was receiving aspirin only.

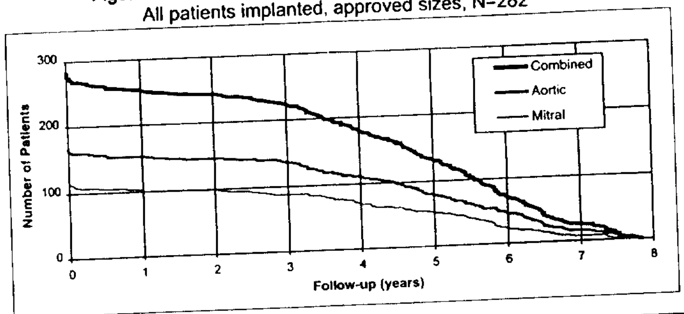
The cohort included 314 patients (172 men, 142 women), aged from 23 to 85 years (mean of 56 years). Cumulative follow-up was 1391 patient-years with mean follow-up of 4.4 patient-years (SD=2.1 years, range = 0-8 years).

Table 7.1: Patient Characteristics
All patients implanted, N=314, 1391 patient years

Description of Patients	Aortic Valve (N=178)	Mitral Valve (N=136)
Age (mean ± SD, N [min., max.])	56±11, 178 [23, 77]	56±11, 136 [30, 84]
Gender (%male/% female)	72%/28%	32%/68%
Etiology of valve disease		
Regurgitation - % of pts. with significant regurgitation (% (number in subgroup/N))	16% (29/178)	18% (24/136)
Stenosis - % of pts. with any stenosis (% (number in subgroup/N))	31% (55/178)	25% (34/136)
Mixed - % of pts. with sign. regurgitation and any stenosis (% (number in subgroup/N))	39% (69/178)	34% (46/136)

Figure 7.1 shows the number of patients implanted *versus* duration of follow-up in the graphic with a breakdown by valve location (aortic and mitral). Table 7.2 shows the number of patients implanted. Table 7.3 shows the duration of follow-up for each valve size and implant location.

Figure 7.1: Number of Patients by Location over Time
All patients implanted, approved sizes, N=282



Year	0	1	2	3	4	5	6	7
Combined	282	253	243	223	180	132	71	26
Aortic	166	152	146	135	111	79	47	17
Mitral	116	101	97	88	69	53	24	9

Table 7.2: Number of Patients Implanted and Number with Hemodynamic Data
By Implant Location and Valve Size, All patients implanted, approved sizes, N=282

Implant location	Valve size (mm)					
	21	23	25	27	29-33	Total
Aortic	30/18	56/16	56/13	20/10	4/4	166/61
Mitral	-	-	-	41/13	75/22	116/35
Total	30/18	56/16	56/13	61/23	79/26	282/96

Table 7.3: Number of Patient-years by Implant Location and Valve Size
By Implant Location and Valve Size, All patients implanted, approved sizes, N=282

Implant location	Valve size (mm)					
	21	23	25	27	29-33	Total
Aortic	112.1	293.1	239.4	97.1	20.6	762
Mitral	-	-	-	179.4	318.7	498
Total	112	293	239	277	339	1260

Table 7.4: Effectiveness Outcomes
All patients catheterized[1]: N = 96, all values reported as: number in subgroup/N, mean ± SD (min, max.)

Endpoint	Pre-op	Early[2]	Late[3]	Annual
Aortic Valve Replacement	All patients implanted: N = 314, all values reported as: number in subgroup/N, mean ± SD (min, max.)			
Functional NYHA	61/61, 3.1 ± 0.7 (2 - 4)	14/61, 1.9 ± 0.9 (1 - 4)	29/61, 1.2 ± 0.4 (1 - 2)	35/61, 1.4 ± 0.6 (1 - 2)
Valvular Regurgitation	—	3/61, 1.3 ± 0.5 (1 - 2)	23/61, 1.1 ± 0.3 (1 - 2)	35/61, 1.1 ± 0.3 (0 - 2)
Valve Gradient[4] (mmHg)				
21mm	—	—	6/61, 12.8 ± 9.7 [0,30]	11/61, 11 ± 3.4 [5,17]
23mm	—	—	4/61, 7.4 ± 3.7 [3,12]	11/61, 9.8 ± 4.0 [3,20]
25mm	—	1/61, 12 ± 0 [n/a]	2/61, 2.5 ± 2.5 [0,5]	5/61, 9.2 ± 2.1 [5,11]
27mm	—	—	5/61, 3.8 ± 3.2 [0,7]	4/61, 7.5 ± 4.3 [0,10]
29mm	—	—	3/61, 3.1 ± 2.6 [0,6.4]	1/61, 6 ± 0 [n/a]
Effective Orifice Area (mm^2)				
21mm	—	—	6/61, 1.5 ± 0.4 [1.1,2.3]	11/61, 1.4 ± 0.2 [1,1.7]
23mm	—	—	4/61, 1.4 ± 0.9 [0.6,3]	11/61, 1.8 ± 0.4 [1.2,2.2]
25mm	—	1/61, 2.3 ± 0 [n/a]	2/61, 2.5 ± 0.2 [2.3,2.7]	5/61, 2.1 ± 0.4 [1.5,2.6]
27mm	—	—	5/61, 2.4 ± 0.8 [1.4,3.9]	4/61, 2.4 ± 0.4 [2,2.8]
29mm	—	—	3/61, 2.2 ± 0.2 [2,2.4]	1/61, 3.5 ± 0 [n/a]
Mitral Valve Replacement				
Functional NYHA	34/35, 3.0 ± 0.5 (1 - 4)	9/35, 2.6 ± 0.8 (1 - 4)	18/35, 1.4 ± 0.6 (1 - 4)	16/35, 1.7 ± 0.8 (1 - 4)
Valvular Regurgitation	—	9/35, 1.3 ± 1.1 (0 - 3)	11/35, 1.1 ± 0.5 (0 - 2)	15/35 1.6 ± 1.1 (1 - 4)
Mean Gradient (mmHg)				
27mm	—	2/35, 7.1± 0.1 [7,7.2]	6/35, 6.3 ± 1.2 [5,8.3]	5/35, 5.4 ± 2.5 [2.7,8.4]
29mm	—	3/35, 2.0 ± 1.4 [0,3]	3/35, 6.3 ± 0.5 [6,7]	5/35, 5.5 ± 6.3 [1.4,18.1]
31mm	—	2/35, 4.6 ± 0.5 [4.1,5]	2/35, 4.5 ± 3.5 [1,8]	3/35, 3.8 ± 1.1 [2.3,5]
33mm	—	—	—	1/35, 12 ± 0 [n/a]
Effective Orifice Area (mm^2)				
27mm	—	2/35, 1.5 ± 0.1 [1.4,1.5]	6/35, 1.9 ± 0.7 [1.2,3.2]	5/35, 2.2 ± 0.7 [1.4,3.3]
29mm	—	2/35, 2.6 ± 0.1 [2.5,2.7]	3/35, 1.6 ± 0.1[1.5,1.7]	5/35, 2.1 ± 0.7 [0.8,2.7]
31mm	—	2/35, 2.6 ± 0.6 [2,3.1]	2/35, 2.4 ± 0.6 [1.8,3]	3/35, 3.3 ± 1.1 [1.9,4.7]

1. Catheterization data was collected on 96 patients (61 aortic, 35 mitral). The majority of these patients (92) came from 7 centers not enrolled in this study
2. Early post-operative evaluation conducted at 30-days post-implantation or hospital discharge.
3. Late post-operative evaluation conducted at 3-6 months post-implantation.
4. The "peak-to-peak" difference between systolic pressure measurements obtained just proximal and distal to a semilunar valve. The mean gradient is used to ... across an atrioventricular valve.

8. INDIVIDUALIZATION OF TREATMENT

8.1 Anticoagulant and/or Antiplatelet Therapy

Adequate anticoagulant and/or antiplatelet therapy should be administered. Selection of an anticoagulant and /or antiplatelet regimen is based on the particular needs of the patient and the clinical situation.

8.2 Specific Patient Populations

The safety and effectiveness of the Monostrut™ Cardiac Prosthesis has not been established for the following specific populations because it has not been studied in these populations:

- patients who are pregnant;
- nursing mothers;
- patients implanted with the Monostrut™ Cardiac Prosthesis for more than 5 years (see CLINICAL STUDIES section 7);
- patients with chronic endocarditis;
- patients requiring pulmonic or tricuspid prosthesis replacement.

There was limited use of the valve in patients requiring double or multiple valve replacement.

9. PATIENT COUNSELING

Patients with prosthetic valves who undergo dental or other potentially bacteremic procedures must be considered for prophylactic antibiotic therapy.

Patients require anticoagulation and /or antiplatelet therapy.

Patients should be encouraged to carry with them at all times a completed Patient ID card provided with the valve.

10. HOW SUPPLIED

Monostrut™ Cardiac Prosthesis is packaged and sterilized in a Double Aseptic Transfer (DAT) package consisting of rigid plastic inner and outer containers with bacterial filters. Each prosthesis is supplied with a PTFE fabric suture ring.

Monostrut™ Cardiac Prosthesis Sizers (REF: BS - Individual Sizer, BSS Sizer Set) are available to the implanting surgeon as an aid in selecting the appropriate prosthesis size. Each set of sizers is packaged with additional instructions for use specific to the prosthesis sizer.

Only handle the prosthesis with a Monostrut™ Cardiac Prosthesis Holder Set (REF: BSMH). The set is supplied with one handle and a series of uniquely identified heads made specifically to correctly hold a series of prosthesis sizes.

Each set of holders is packaged with additional instructions for use specific to the prosthesis holder. If the prosthesis requires rotation after it is sutured in place, it may be rotated by re-inserting the holder head and turning it within the suture ring.

11. DIRECTIONS FOR USE

11.1 Physician Training

Surgical implantation technique may affect the function of the prosthetic valve.[2]

Implanting physicians must be familiar with the techniques for implanting Monostrut™ Cardiac Prosthesis (see Monostrut™ Training Manual).

11.2 Prosthesis handling

Carefully examine the seals of the outer and inner packages. If the integrity of <u>any</u> safety seal or bacterial filter has been compromised, the prosthesis must be resterilized. The prosthesis should be stored and resterilized in its original inner container to avoid damage.

1. The exposed inner container is sterile. The bottom portion of the DAT package is removed by circulating (non-sterile) personnel to expose the sterile inner container.
2. The inner container is removed by operating (sterile) personnel.
3. After transferring the inner container to the sterile field, remove the lid, and place the prosthesis on the appropriate sized holder head. USE EXTREME CARE WHEN PLACING THE PROSTHESIS ON THE HOLDER TO ENSURE CORRECT POSITIONING FOR INSERTION. Refer to Figures 1 and 2 for a correctly positioned aortic prosthesis and to Figures 3 and 4 for a correctly positioned mitral prosthesis.

Figures 1-4. Aortic Prosthesis & Holder, Mitral Prosthesis & Holder

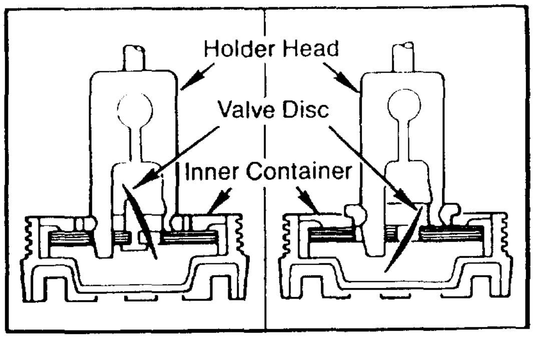


Figure 1. Aortic Prosthesis   Figure 3. Mitral Prosthesis

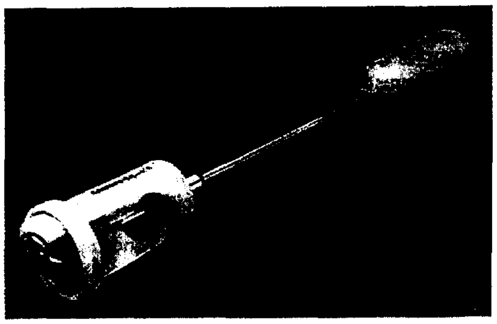


Figure 2. Properly Positioned Aortic Prosthesis

11.3 Aortic Prosthesis (Figures 1 and 2)

1) Insert the appropriate size holder fingers into the orifice ring from the outflow side of the prosthesis by positioning the larger finger under the opened disc, then rock the smaller finger into position. Holder fingers may be squeezed to facilitate attachment of the prosthesis.

2) Rotate the handle clockwise in the holder head to secure the prosthesis. EXCESSIVE TIGHTENING MAY CAUSE THE PROSTHESIS TO EJECT FROM THE HOLDER.

3) The prosthesis, attached to the holder head, can now be removed from the inner container.

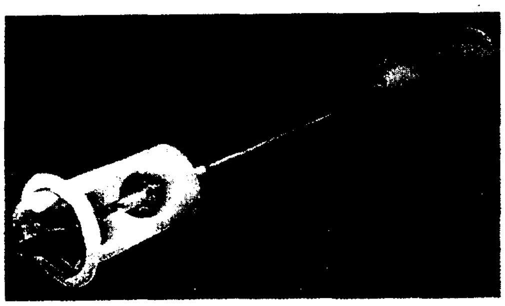


Figure 4. Properly Positioned Mitral Prosthesis

11.4 Mitral Prosthesis (Figures 3 and 4)

1) Insert the appropriate size holder fingers into the orifice ring from the inflow side of the prosthesis by positioning the smaller finger into the orifice ring, then rock the larger finger into position. Holder fingers may be squeezed to facilitate attachment of the prosthesis.

2) Rotate the handle clockwise in the holder head to ensure a secure attachment to the prosthesis. EXCESSIVE TIGHTENING MAY CAUSE THE PROSTHESIS TO EJECT FROM THE HOLDER.

3) Remove the secured prosthesis from the inner container.

4) To avoid risk of atrioventricular disruption, it is suggested that the mitral prosthesis selected be one size smaller than the measured tissue annulus.[3]

11.5 Serial Number Tag

Verify that the sewing ring serial number tag corresponds with the inner container label and the implant data card.

Record the serial number in the patient's file. Do not remove the serial number tag attached to the sewing ring until the surgeon decides on a particular size prosthesis and secures it on the holder. This will prevent sizing error when more than one prosthesis is in the sterile field. REMOVE THE SERIAL NUMBER TAG FROM THE PROSTHESIS.

1) Grasp the HEAD PORTION OF THE HOLDER with one hand and the sewing ring with the other as depicted in Figure 5. Use sterile gauze to keep the prosthesis clean.

Figure 5. Correct Technique for Sewing Ring Rotation

2) Rotate the prosthesis at least 5 full revolutions within the sewing ring prior to suture placement to ensure its freedom to rotate in situ.

The holder must be used to rotate the prosthesis after it has been sutured in place.

If an antibiotic pre-soak is desired, a dilute solution of penicillin and heparin may be used.

Valve orientation should ensure unimpeded disc movement. This is usually achieved with the disc opening into the ventricular outflow tract (mitral valve), or into the aortic sinus (aortic valve)

11.6 Resterilization Guidelines

If the lid of the inner container is removed, check the disc of the prosthesis to see if it is positioned correctly. Refer to Figures 6 and 7 for correct aortic and mitral disc positioning. Replace the lid on the inner container and ensure that the disc fits into the lid insert hole.

A method of tracking the number of resterilizations must be in place if resterilization is used.

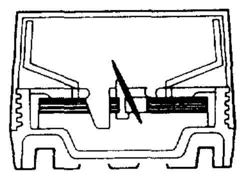


Figure 6. Aortic Position

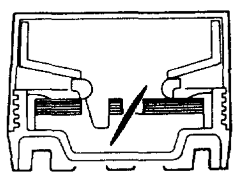


Figure 7. Mitral Position

Steam Resterilization-

1. Do not steam sterilize in the original outer container. The inner container must be placed in a breathable, autoclavable pouch and sealed.
2. Autoclave at: 250°F (121°C) and 15 psig (1.0 Kg/cm2) for 40 minutes minimum.
3. Steam sterilization destroys the bacterial filter.
4. Store the sterilized package in a cool, dry place.

Ethylene Oxide Sterilization (100%EtO):
The inner container must be placed in a sealed, breathable pouch.

1. The inner container must be placed in a breathable pouch and sealed.
2. Sterilize in 100% EtO as follows

Preconditioning-	Temperature: 110° ± 10° F Time: 24 hours. Relative humidity: 45-75%
Gas exposure-	Temperature: 120° ± 10° F Time: 5 to 6 hours. Pressure: 11.7 ± 5 inHg (5.7 ± 2 psig)
EtO-	601 – 701 mg/L min.

3. Aerate the package for six days at room temperature or for 12 hours at 120° in a mechanical aerator.
4. Store the sterilized package in a cool, dry place.

12. POSTOPERATIVE INFORMATION

12.1 Compatibility with MRI

Monostrut™ Cardiac Prosthesis is compatible with magnetic resonance systems.[4]

12.2 Returned Goods Policy

For detailed information on the Alliance Medical Technologies, Inc. returned goods policy, please contact your local Alliance representative.

12.3 Return of Explanted Prosthetic Valves

Alliance Medical Technologies, Inc. is extremely interested in obtaining recovered clinical specimens of the Monostrut™ Cardiac Prosthesis. Specific studies of the explant will be determined by the Alliance Review Board under the direction a consulting pathologist. A written report summarizing the findings will be returned to you. Please contact Alliance Medical Technologies to obtain a Product Return Kit and Return Product Report Number (RPR#), protocol and explant pathology information form. The explanted valve should be placed, completely submersed in a 2-5% formalin solution immediately after excision unless otherwise directed by your Alliance representative.

13. PATIENT INFORMATION

13.1 Implantation Data Card

The Implantation Data Card provides vital prosthesis implantation data. After recording all information requested detach lower portions of the card to provide implantation records for the surgeon and an implantation identification card for the patient. Return the completed Implantation Data Card to Alliance Medical Technologies, Inc.

13.2 Patient's Manual

Prior to hospital discharge, the patient should receive the Alliance Medical Technologies patient brochure.

14. REFFRENCES

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3. Williams, Donald B. et al, "Extrinsic Obstruction of the Björk-Shiley Prosthesis in the Mitral Position", Annals of Thoracic Surgery, Vol. 32, No. 1, July 1981, P. 58.
4. Randall, Patricia A., M.D., et al, "Magnetic Resonance Imaging of Prosthetic Cardiac Prosthesis in Vitro and In Vivo", The American Journal of Cardiology, Vol. 62, November 1988.

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US Patent Nos. 4,057,857; 4,276,132; 4,343,049
DPO2-0407-001G